

Naval Medical Center Portsmouth (NMCP) COVID-19 Literature Report

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, special reports, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the [list of retracted papers from Retraction Watch](#).

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A Brief Note and Request

The NMCP COVID-19 Literature Report has been produced for over 2 years. What started out as temporary and short document to share information on an emerging disease has evolved to a long form collection of COVID-related items from a variety of sources.

These reports take significant time and effort to produce. As the 100th issue approaches, I want to touch base with the people who read the reports and ask:

- What value do these report have to you? Have they made a difference in decision making or impacted patient care?
- Should these reports continue?
- If they do, how can they best support what you need?

I welcome your opinions, suggestions, or any other constructive feedback regarding these reports; please email usn.hampton-roads.navhospvorsva.list.nmcp-library@mail.mil. Thank you!

The Big Picture

News in Brief

Grim Milestones

"One million of us" ([WP](#)).

Here is what one million Covid deaths in the U.S. looks like" ([Forbes](#)).

"15 million people have died in the pandemic, WHO says" ([Nature](#); see also: [WHO report](#)).

"The 'five pandemics' driving 1 million U.S. Covid deaths" ([STAT](#)).

"After 1 million deaths, covid leaves millions more forever changed" ([WP](#)).

"Few eligible families have sought federal payment of COVID funeral expenses" (NPR).

Surges

"Are COVID surges becoming more predictable? New Omicron variants offer a hint" ([Nature](#)).

"America is starting to see what COVID immunity really looks like: With time and effort, we can build enough protection to blunt surges—but herd immunity remains out of reach" ([Atlantic](#)).

"North Korea admits to coronavirus outbreak for the first time" ([WP](#)). Followed by: "North Korea announces first Covid deaths amid 'explosive' outbreak" ([CNN](#)).

Webinars and Events

WHAT: [What Happened to the Plans? Lessons Observed from COVID-19 - A Workshop](#)

WHEN: Tuesday, 17 May 2022 0900–1630 EDT
Wednesday, 18 May 2022 0900–1540 EDT

DETAILS: The National Academies of Sciences, Engineering, and Medicine will organize and convene a two-day in person public workshop where invited speakers will explore the nation's Public Health Emergency (PHE) preparedness & response enterprise through the lens the COVID-19 response in the United States.

The workshop will explore key components, success stories, as well as failure points throughout the entire PHE preparedness and response enterprise in order to identify opportunities for more effective catastrophic disaster, pandemic, and other large scale PHEs planning at the federal, state, local, tribal, and territorial levels. Specifically, the workshop will examine weaknesses and opportunities in the PHE's systems architecture, including but not limited to:

- Global disease surveillance;
- Medical Supply chain and Medical Counter Measure (MCM) viability and vulnerabilities;
- The continuum of local-state-regional-national coordination challenges and leadership incident command structure disparities,
- Preparedness and response capabilities, authorities, and funding streams; and
- Engaging with vulnerable populations, risk communication and messaging failures.

Special Reports and Other Resources

NASEM: [Rapid Expert Consultation on Critical Federal Capabilities Needed to Evaluate Real-World Safety, Effectiveness, and Equitable Distribution and Use of Medical Countermeasures During a Public Health Emergency](#) (May 2022)

"The COVID-19 pandemic has highlighted the importance of having access to real-world data and evidence to monitor and assess medical countermeasure (MCM) use and performance so policy makers can make more effective and rapid public health decisions, protect population health, and save lives. During public health emergencies, the use of MCMs, such as therapeutics, vaccines, and diagnostics, can be made available to the public under a range of regulatory access mechanisms."

Journal Articles

Disaster Med Public Health Prep: [The Role of Public Health Emergency Management in Biodefense: A COVID-19 Case Study](#) (02 May 2022)

"The emergence of COVID-19 pandemic has had significant impacts on human lives as well as economic and social stability. The United States has a complicated history with biosecurity as policymaking, biodefense activities and government transparency have historically been in contention (Vogel, 2008). The September 11th terror attacks uncovered various weaknesses in the national public health infrastructure that have persisted into the current pandemic. This study explores the biodefense and public health preparedness landscape for trends in federal support and capacity building. The study investigates the applicability of public health emergency management principles to the biodefense structure. Results included identification of eight common themes of failure during the COVID-19 response; (1) accountable leadership, (2) statutory authorities and policies, (3) interagency coordination, (4) coherent data system for situational awareness, (5) strategic national stockpile and supply chain, (6) testing and surveillance, (7) health care system surge capacity and resilience, and (8) federal funds, and the role of public health emergency management in the evolving landscape of biothreats, both intentional and natural. To counter the increasing biothreats, the United States must invest in revamping the biodefense infrastructure to mimic and support public health emergency preparedness initiatives which will increase our resilience to various biothreats."

PLoS One: [COVID-19 mortality in the United States: It's been two Americas from the start](#) (28 April 2022)

"During the summer of 2021, a narrative of "two Americas" emerged: one with high demand for the COVID-19 vaccine and the second with widespread vaccine hesitancy and opposition to masks and vaccines. We analyzed "excess mortality" rates (the difference between total deaths and what would have been expected based on earlier time periods) prepared by the CDC for the United States from January 3, 2020 to September 26, 2021. Between Jan. 3, 2020 and Sept. 26, 2021, there were 895,693 excess deaths associated with COVID-19, 26% more than reported as such. The proportion of deaths estimated by the excess mortality method that was reported as COVID-19 was highest in the Northeast (92%) and lowest in the West (72%) and South (76%). Of the estimated deaths, 43% occurred between Oct. 4, 2020 and Feb. 27, 2021. Before May 31, 2020, approximately 56% of deaths were in the Northeast, where 17% of the population resides. Subsequently, 48% of deaths were in the South, which makes up 38% of the population. Since May 31, 2020, the South experienced COVID-19 mortality 26% higher than the national rate, whereas the Northeast's rate was 42% lower. If each region had the same mortality rate as the Northeast, more than 316,234 COVID-19 deaths between May 31, 2020 and Sept. 26, 2021 were "avoidable." More than half (63%) of the avoidable deaths occurred between May 31, 2020 and

February, 2021, and more than half (60%) were in the South. Regional differences in COVID-19 mortality have been strong throughout the pandemic. The South has had higher mortality rates than the rest of the U.S. since May 31, 2020, and experienced 62% of the avoidable deaths. A comprehensive COVID-19 policy, including population-based restrictions as well as vaccines, is needed to control the pandemic."

SARS-CoV-2 Virus and Variants

News in Brief

"Virus mutations aren't slowing down. New omicron subvariant proves it" ([WP](#)).

"More uniformly infectious, more treatable, more genetically predictable: How coronavirus is getting closer to flu" ([STAT](#)).

Long Reads

"The pros and cons of giving people COVID for science: Should the first COVID human challenge trial also be the last?" ([Slate](#))

Transmission, Exposure, and Surveillance

News in Brief

"Most COVID transmission is still asymptomatic — some 60% of spread starts with those who have no symptoms, and that may be higher with Omicron" ([Medpage](#)).

"What the current spike in Covid-19 cases could say about the coronavirus' future" ([STAT](#)).

"The lucky few to never get coronavirus could teach us more about it: Scientists turn their attention to finding the rare individuals who have not yet contracted the virus" ([WP](#)).

Journal Articles

Int J Infect Dis: [The Role of Children in Household Transmission of COVID-19: A Systematic Review and Meta-Analysis](#) (10 May 2022)

"Background: Household is potentially the highest-risk exposure setting of SARS-COV-2 transmission, in which the role of children has remained controversial.

Methods: Through retrieval in PubMed and EMBASE, studies were included in two parts: meta-analysis of the household secondary attack rate (SAR) and case analysis of household pediatric infections.

Results: A total of 95 articles were included: 48 for meta-analysis and 47 for case analysis. Pediatric COVID-19 only comprised a minority of the household transmission. The total pooled household SAR of child index cases and contacts were 0.20 (95% CI: 0.15-0.26) and 0.24 (95% CI: 0.18-0.30). Lower household transmissibility was reported in both child index cases and contacts compared to adults (RR = 0.64, 95% CI: 0.50-0.81; RR=0.74, 95% CI: 0.64-0.85). Younger children were as susceptible as the older children (RR=0.89, 95% CI: 0.72-1.10). Through subgroup analyses of different variants and periods, increased household SAR was observed in children (Wild: 0.20; Alpha: 0.42; Delta: 0.35; Omicron: 0.56) and no significant difference was found in household SAR between children and adults when new variants dominated.

Conclusions: Although children were demonstrated not to be dominant in the household transmission, their transmissibility of SARS-CoV-2 appeared on the rise as new variants emerge."

Nat Med: [Modeling transmission of SARS-CoV-2 Omicron in China](#) (10 May 2022)

"Having adopted a dynamic zero-COVID strategy to respond to SARS-CoV-2 variants with higher transmissibility since August 2021, China is now considering whether and for how long this policy can remain in place. The debate has thus shifted towards the identification of mitigation strategies for minimizing disruption to the healthcare system in the case of a nationwide epidemic. To this aim, we developed an age-structured stochastic compartmental susceptible-latent-infectious-removed-susceptible (SLIRS) model of SARS-CoV-2 transmission calibrated on the initial growth phase for the 2022 Omicron outbreak in Shanghai, to project COVID-19 burden (i.e., number of cases, patients requiring hospitalization and intensive care, and deaths) under hypothetical mitigation scenarios. The model also considers age-specific vaccine coverage data, vaccine efficacy against different clinical endpoints, waning of immunity, different antiviral therapies, and non-pharmaceutical interventions. We find that the level of immunity induced by the March 2022 vaccination campaign would be insufficient to prevent an Omicron wave that would result in exceeding critical care capacity with a projected intensive care unit peak demand of 15.6-times the existing capacity and causing approximately 1.55 million deaths. However, we also estimate that protecting vulnerable individuals by ensuring accessibility to vaccines and antiviral therapies, and maintaining implementation of non-pharmaceutical interventions could be sufficient to prevent overwhelming the healthcare system, suggesting that these factors should be points of emphasis in future mitigation policies."

Nat Microbiol: [Daily longitudinal sampling of SARS-CoV-2 infection reveals substantial heterogeneity in infectiousness](#) (07 May 2022)

"The dynamics of SARS-CoV-2 replication and shedding in humans remain poorly understood. We captured the dynamics of infectious virus and viral RNA shedding during acute infection through daily longitudinal sampling of 60 individuals for up to 14 days. By fitting mechanistic models, we directly estimated viral expansion and clearance rates and overall infectiousness for each individual. Significant person-to-person variation in infectious virus shedding suggests that individual-level heterogeneity in viral dynamics contributes to 'superspreading'. Viral genome loads often peaked days earlier in saliva than in nasal swabs, indicating strong tissue compartmentalization and suggesting that saliva may serve as a superior sampling site for early detection of infection. Viral loads and clearance kinetics of Alpha (B.1.1.7) and previously circulating non-variant-of-concern viruses were mostly indistinguishable, indicating that the enhanced transmissibility of this variant cannot be explained simply by higher viral loads or delayed clearance. These results provide a high-resolution portrait of SARS-CoV-2 infection dynamics and implicate individual-level heterogeneity in infectiousness in superspreading."

Open Forum Infect Dis: [Detection of SARS-CoV-2 by Canine Olfaction: A Pilot Study](#) (07 May 2022)

"Background: As the number of COVID-19 cases continue to surge worldwide and new variants emerge, additional accurate, rapid, and non-invasive screening methods to detect SARS-CoV-2 are needed. The number of COVID-19 cases reported globally is over 455 million and deaths have surpassed 6 million. Current diagnostic methods are expensive, invasive, and produce delayed results. While COVID-19 vaccinations are proven to help slow the spread of infection and prevent serious illness, they are not equitably available worldwide. Almost 40% of the world's population remains unvaccinated. Evidence suggests that SARS-CoV-2 virus-associated volatile organic compounds found in the breath, urine, and sweat of infected individuals can be detected by canine olfaction. Medical detection dogs may be a feasible, accurate and affordable SARS-CoV-2 screening method.

Methods: In this double-blinded, case-control, validation study, we obtained sweat samples from inpatients and outpatients tested for SARS-CoV-2 by a polymerase chain reaction test. Medical detection dogs were trained to distinguish SARS CoV-2 positive samples from SARS-CoV-2 negative samples, using reward-based reinforcement.

Results: Samples were obtained from 584 individuals (6 to 97 years of age; 24% positive SARS CoV-2 samples and 76% negative SARS CoV-2 samples). In the Testing Phase, all dogs performed with high accuracy in detecting SARS-CoV-2: overall diagnostic sensitivity was 98% and specificity was 92%. In a follow-up phase, one dog screened 153 patients for SARS-CoV-2 in a hospital setting with 96% diagnostic sensitivity and 100% specificity.

Conclusions: Canine olfaction is an accurate and feasible method for diagnosis of SARS-CoV-2, including asymptomatic and pre-symptomatic infected individuals."

Sci Rep: [Excretion and viability of SARS-CoV-2 in feces and its association with the clinical outcome of COVID-19](#) (05 May 2022)

"The main objective was to evaluate the viability of the SARS-CoV-2 viral particles excreted in stools. In addition, we aimed to identify clinical factors associated with the detection of SARS-CoV-2 RNA in feces, and to determine if its presence is associated with an unfavorable clinical outcome, defined as intensive care unit (ICU) admission and/or death. A prospective multicenter cohort study of COVID-19 adult patients, with confirmed SARS-CoV-2 infection by RT-PCR assay in nasopharyngeal (NP) swabs admitted to four hospitals in Spain, from March 2020 to February 2021. Sixty-two adult COVID-19 patients had stool samples collected at admission and/or during the follow up, with a total of 79 stool samples. SARS-CoV-2 RNA was detected in stool samples from 27 (43.5%) out of the 62 patients. Replicative virus, measured by the generation of cytopathic effect in cell culture and subsequent RT-PCR confirmation of a decrease in the Ct values, was not found in any of these stool samples. Fecal virus excretion was not associated with the presence of gastrointestinal symptoms, or with differences in the evolution of COVID-19 patients. Our results suggest that SARS-CoV-2 replicative capacity is null or very limited in stool samples, and thus, the fecal-oral transmission of SARS-CoV-2 as an alternative infection route is highly unlikely. In our study, the detection of SARS-CoV-2 RNA in feces at the beginning of the disease is not associated with any clinical factor nor with an unfavorable clinical outcome."

COVID-19 Vaccines

News in Brief

"White House documents detail a looming squeeze on Covid-19 boosters" ([STAT](#)).

"The number of Americans who say they won't get a COVID shot hasn't budged in a year" ([NPR](#)).

"Nose spray vaccines could quash COVID virus variants: Three nasal spritzes, now in advanced trials, could trigger stronger immunity than shots in the arm" ([SciAm](#)).

Journal Articles

Clin Infect Dis: [Antibody response of heterologous vs homologous mRNA vaccine boosters against the SARS-CoV-2 Omicron variant: interim results from the PRIBIVAC study, A Randomized Clinical Trial](#) (11 May 2022)

"Background: Waning antibody levels post-vaccination and the emergence of variants of concern (VOCs) capable of evading protective immunity has raised the need for booster vaccinations. However, which combination of COVID-19 vaccines offers the strongest immune response against Omicron variant is unknown.

Methods: This randomized, subject-blinded, controlled trial assessed the reactogenicity and immunogenicity of different COVID-19 vaccine booster combinations. 100 BNT162b2-vaccinated individuals were enrolled and randomized 1: 1 to either homologous (BNT162b2 + BNT162b2 + BNT162b2; 'BBB') or heterologous mRNA booster vaccine (BNT162b2 + BNT162b2 + mRNA-1273; 'BBM'). Primary endpoint was the level of neutralizing antibodies against SARS-CoV-2 wild-type and VOCs at Day 28.

Results: 51 participants were allocated to BBB and 49 to BBM; 50 and 48 respectively were analyzed for safety and immunogenicity outcomes. At Day 28 post-boost, mean SARS-CoV-2 spike antibody titers were lower with BBB (22,382 IU/mL 95% CI, 18,210 to 27,517) vs BBM (29,751 IU/mL 95% CI, 25,281 to 35,011, $p = 0.034$) as was the median level of neutralizing antibodies: BBB 99.0% (IQR 97.9 to 99.3%) vs BBM 99.3% (IQR 98.8 to 99.5%, $p = 0.021$). On sub-group analysis, significant differences in mean spike antibody titer and live Omicron neutralization titer was only observed in older adults. Median surrogate neutralizing antibody level against all VOCs was also significantly higher with BBM in older adults, and against Omicron was BBB 72.8% (IQR 54.0 to 84.7%) vs BBM 84.3% (IQR 78.1 to 88.7%, $p = 0.0073$). Both vaccines were well tolerated.

Conclusions: Heterologous mRNA-1273 booster vaccination induced a stronger neutralizing response against the Omicron variant in older individuals compared with homologous BNT123b2."

NEJM: [Protection by a Fourth Dose of BNT162b2 against Omicron in Israel](#) (05 May 2022)

"Background: On January 2, 2022, Israel began administering a fourth dose of BNT162b2 vaccine to persons 60 years of age or older. Data are needed regarding the effect of the fourth dose on rates of confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and of severe coronavirus disease 2019 (Covid-19).

Methods: Using the Israeli Ministry of Health database, we extracted data on 1,252,331 persons who were 60 years of age or older and eligible for the fourth dose during a period in which the B.1.1.529 (omicron) variant of SARS-CoV-2 was predominant (January 10 through March 2, 2022). We estimated the rate of confirmed infection and severe Covid-19

as a function of time starting at 8 days after receipt of a fourth dose (four-dose groups) as compared with that among persons who had received only three doses (three-dose group) and among persons who had received a fourth dose 3 to 7 days earlier (internal control group). For the estimation of rates, we used quasi-Poisson regression with adjustment for age, sex, demographic group, and calendar day.

Results: The number of cases of severe Covid-19 per 100,000 person-days (unadjusted rate) was 1.5 in the aggregated four-dose groups, 3.9 in the three-dose group, and 4.2 in the internal control group. In the quasi-Poisson analysis, the adjusted rate of severe Covid-19 in the fourth week after receipt of the fourth dose was lower than that in the three-dose group by a factor of 3.5 (95% confidence interval [CI], 2.7 to 4.6) and was lower than that in the internal control group by a factor of 2.3 (95% CI, 1.7 to 3.3). Protection against severe illness did not wane during the 6 weeks after receipt of the fourth dose. The number of cases of confirmed infection per 100,000 person-days (unadjusted rate) was 177 in the aggregated four-dose groups, 361 in the three-dose group, and 388 in the internal control group. In the quasi-Poisson analysis, the adjusted rate of confirmed infection in the fourth week after receipt of the fourth dose was lower than that in the three-dose group by a factor of 2.0 (95% CI, 1.9 to 2.1) and was lower than that in the internal control group by a factor of 1.8 (95% CI, 1.7 to 1.9). However, this protection waned in later weeks.

Conclusions: Rates of confirmed SARS-CoV-2 infection and severe Covid-19 were lower after a fourth dose of BNT162b2 vaccine than after only three doses. Protection against confirmed infection appeared short-lived, whereas protection against severe illness did not wane during the study period."

NEJM: [Efficacy and Safety of a Recombinant Plant-Based Adjuvanted Covid-19 Vaccine](#) (04 May 2022)

"Background: Coronavirus-like particles (CoVLP) that are produced in plants and display the prefusion spike glycoprotein of the original strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are combined with an adjuvant (Adjuvant System 03 [AS03]) to form the candidate vaccine.

Methods: In this phase 3, multinational, randomized, placebo-controlled trial conducted at 85 centers, we assigned adults (≥ 18 years of age) in a 1:1 ratio to receive two intramuscular injections of the CoVLP+AS03 vaccine or placebo 21 days apart. The primary objective of the trial was to determine the efficacy of the CoVLP+AS03 vaccine in preventing symptomatic coronavirus disease 2019 (Covid-19) beginning at least 7 days after the second injection, with the analysis performed after the detection of at least 160 cases.

Results: A total of 24,141 volunteers participated in the trial; the median age of the participants was 29 years. Covid-19 was confirmed by polymerase-chain-reaction assay in 165 participants in the intention-to-treat population; all viral samples that could be

sequenced contained variants of the original strain. Vaccine efficacy was 69.5% (95% confidence interval [CI], 56.7 to 78.8) against any symptomatic Covid-19 caused by five variants that were identified by sequencing. In a post hoc analysis, vaccine efficacy was 78.8% (95% CI, 55.8 to 90.8) against moderate-to-severe disease and 74.0% (95% CI, 62.1 to 82.5) among the participants who were seronegative at baseline. No severe cases of Covid-19 occurred in the vaccine group, in which the median viral load for breakthrough cases was lower than that in the placebo group by a factor of more than 100. Solicited adverse events were mostly mild or moderate and transient and were more frequent in the vaccine group than in the placebo group; local adverse events occurred in 92.3% and 45.5% of participants, respectively, and systemic adverse events in 87.3% and 65.0%. The incidence of unsolicited adverse events was similar in the two groups up to 21 days after each dose (22.7% and 20.4%) and from day 43 through day 201 (4.2% and 4.0%).

Conclusions: The CoVLP+AS03 vaccine was effective in preventing Covid-19 caused by a spectrum of variants, with efficacy ranging from 69.5% against symptomatic infection to 78.8% against moderate-to-severe disease."

Nat Commun: [Comparative effectiveness over time of the mRNA-1273 \(Moderna\) vaccine and the BNT162b2 \(Pfizer-BioNTech\) vaccine](#) (02 May 2022)

"Real-world analysis of the incidence of SARS-CoV-2 infection post vaccination is important in determining the comparative effectiveness of the available vaccines. In this retrospective cohort study using deidentified administrative claims for Medicare Advantage and commercially insured individuals in a research database we examine over 3.5 million fully vaccinated individuals, including 8,848 individuals with SARS-CoV-2 infection, with a follow-up period between 14 and 151 days after their second dose. Our primary outcome was the rate of Covid-19 infection occurring at 30, 60, and 90 days at least 14 days after the second dose of either the mRNA-1273 vaccine or the BNT162b2 vaccine. Sub-analyses included the incidence of hospitalization, ICU admission, and death/hospice transfer. Separate analysis was conducted for individuals above and below age 65 and those without a prior diagnosis of Covid-19. We show that immunization with mRNA-1273, compared to BNT162b2, provides slightly more protection against SARS-CoV-2 infection that reaches statistical significance at 90 days with a number needed to vaccinate of >290. There are no differences in vaccine effectiveness for protection against hospitalization, ICU admission, or death/hospice transfer (aOR 1.23, 95% CI (0.67, 2.25))."

BMJ Mil Health: [Vaccine efficacy against the SARS-CoV-2 Delta variant during a COVID-19 outbreak aboard a military ship](#) (29 April 2022)

"We report the investigation of a COVID-19 outbreak that occurred among the 91 crew members of a French Navy ship from May to July 2021. Before the mission, 87% of the crew were immune: 57% were fully vaccinated with the BNT162b2 vaccine in April–May 2021,

30% had had a previous SARS-CoV-2 infection less than three months before (Alpha or Beta variants) and were not vaccinated (recovered), and 13% had no immunity at all. All had been tested with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and were negative, so that face masks were not mandatory on board."

Breakthrough Infections, Reinfections, and Coinfections

Journal Articles

Antimicrob Steward Healthc Epidemiol: [Coinfections and antimicrobial use in patients hospitalized with coronavirus disease 2019 \(COVID-19\) across a single healthcare system in New York City: A retrospective cohort study](#) (10 May 2022)

"Background and objective: With the coronavirus disease 2019 (COVID-19) pandemic, rates of in-hospital antimicrobial use increased due to perceived bacterial and fungal coinfections along with COVID-19. We describe the incidence of these coinfections and antimicrobial use in patients hospitalized with COVID-19 to help guide effective antimicrobial use in this population.

Setting: This study was conducted in 3 tertiary-care referral university teaching hospitals in New York City.

Methods: This multicenter retrospective observational cohort study involved all patients admitted with COVID-19 from January 1, 2020, to February 1, 2021. Variables of interest were extracted from a de-identified data set of all COVID-19 infections across the health system. Population statistics are presented as median with interquartile range (IQR) or proportions with 95% confidence intervals (CIs) as indicated.

Results: Among 7,209 of patients admitted with COVID-19, 663 (9.2%) had a positive culture from the respiratory tract or blood sometime during their initial hospital admission. Positive respiratory cultures occurred found in 449 (6.2%) patients, and 20% were collected within 48 hours of admission. Blood culture positivity occurred in 334 patients (4.6%), with 33.5% identified within 48 hours of admission. A higher proportion of patients received antimicrobials in the first wave than in the later pandemic period (82.4% vs 52.0%). Antimicrobials were prescribed to 70.1% of inpatients, with a median of 6 antimicrobial days per patient. Infection-free survival decreased over the course of hospitalization.

Conclusions: We detected a very low incidence of coinfection with COVID-19 at admission. A longer duration of hospitalization was associated with an increased risk of coinfection. Antimicrobial use far exceeded the true incidence and detection of coinfections in these patients."

Treatments and Management

News in Brief

"FDA approves Lilly and Incyte's OLUMIANT® (baricitinib) for the treatment of certain hospitalized patients with COVID-19" ([Lilly](#)).

"3 ways to get COVID pills, if you've just tested positive" ([NPR](#)).

"Interferon therapy shows striking results against COVID-19: Given early, one shot sliced hospitalization risk by half in large trial" ([Science](#)).

Paxlovid

"Paxlovid's failure as a preventative measure raises questions, but doctors still back it as a therapeutic" ([STAT](#)).

"Paxlovid mouth is real—and gross: 'I imagine this is what grapefruit juice mixed with soap would taste like.'" ([Atlantic](#)).

"Prisons didn't prescribe much Paxlovid or other Covid-19 treatments, even when they got the drugs" ([STAT](#)).

Journal Articles

BMJ: [Agreement of treatment effects from observational studies and randomized controlled trials evaluating hydroxychloroquine, lopinavir-ritonavir, or dexamethasone for covid-19: meta-epidemiological study](#) (10 May 2022)

"Objective: To systematically identify, match, and compare treatment effects and study demographics from individual or meta-analysed observational studies and randomized controlled trials (RCTs) evaluating the same covid-19 treatments, comparators, and outcomes.

Design: Meta-epidemiological study.

Data sources: National Institutes of Health Covid-19 Treatment Guidelines, a living review and network meta-analysis published in The BMJ, a living systematic review with meta-analysis and trial sequential analysis in PLOS Medicine (The LIVING Project), and the Epistemonikos "Living OVERview of Evidence" (L-OVE) evidence database.

Eligibility criteria for selection of studies: RCTs in The BMJ's living review that directly compared any of the three most frequently studied therapeutic interventions for covid-19 across all data sources (that is, hydroxychloroquine, lopinavir-ritonavir, or dexamethasone)

for any safety and efficacy outcomes. Observational studies that evaluated the same interventions, comparisons, and outcomes that were reported in The BMJ's living review.

Data extraction and synthesis: Safety and efficacy outcomes from observational studies were identified and treatment effects for dichotomous (odds ratios) or continuous (mean differences or ratios of means) outcomes were calculated and, when possible, meta-analyzed to match the treatment effects from individual RCTs or meta-analyses of RCTs reported in The BMJ's living review with the same interventions, comparisons, and outcomes (that is, matched pairs). The analysis compared the distribution of study demographics and the agreement between treatment effects from matched pairs. Matched pairs were in agreement if both observational and RCT treatment effects were significantly increasing or decreasing ($P < 0.05$) or if both treatment effects were not significant ($P \geq 0.05$).

Results: 17 new, independent meta-analyses of observational studies were conducted that compared hydroxychloroquine, lopinavir-ritonavir, or dexamethasone with an active or placebo comparator for any safety or efficacy outcomes in covid-19 treatment. These studies were matched and compared with 17 meta-analyses of RCTs reported in The BMJ's living review. 10 additional matched pairs with only one observational study and/or one RCT were identified. Across all 27 matched pairs, 22 had adequate reporting of demographical and clinical data for all individual studies. All 22 matched pairs had studies with overlapping distributions of sex, age, and disease severity. Overall, 21 (78%) of the 27 matched pairs had treatment effects that were in agreement. Among the 17 matched pairs consisting of meta-analyses of observational studies and meta-analyses of RCTs, 14 (82%) were in agreement; seven (70%) of the 10 matched pairs consisting of at least one observational study or one RCT were in agreement. The 18 matched pairs with treatment effects for dichotomous outcomes had a higher proportion of agreement ($n=16$, 89%) than did the nine matched pairs with treatment effects for continuous outcomes ($n=5$, 56%).

Conclusions: Meta-analyses of observational studies and RCTs evaluating treatments for covid-19 have summary treatment effects that are generally in agreement. Although our evaluation is limited to three covid-19 treatments, these findings suggest that meta-analyzed evidence from observational studies might complement, but should not replace, evidence collected from RCTs."

Sci Rep: [Estimating and explaining cross-country variation in the effectiveness of non-pharmaceutical interventions during COVID-19](#) (09 May 2022)

"To control the COVID-19 pandemic, countries around the world have implemented non-pharmaceutical interventions (NPIs), such as school closures or stay-at-home orders. Previous work has estimated the effectiveness of NPIs, yet without examining variation in NPI effectiveness across countries. Based on data from the first epidemic wave of [Formula: see text] countries, we estimate country-specific differences in the effectiveness of NPIs via

a semi-mechanistic Bayesian hierarchical model. Our estimates reveal substantial variation between countries, indicating that NPIs have been more effective in some countries (e. g. Switzerland, New Zealand, and Iceland) as compared to others (e. g. Singapore, South Africa, and France). We then explain differences in the effectiveness of NPIs through 12 country characteristics (e. g. population age, urbanization, employment, etc.). A positive association with country-specific effectiveness of NPIs was found for government effectiveness, gross domestic product (GDP) per capita, population ages 65+, and health expenditures. Conversely, a negative association with effectiveness of NPIs was found for the share of informal employment, average household size and population density. Overall, the wealth and demographic structure of a country can explain variation in the effectiveness of NPIs."

Lancet: [Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses](#) (02 May 2022)

"Background: The Solidarity trial among COVID-19 inpatients has previously reported interim mortality analyses for four repurposed antiviral drugs. Lopinavir, hydroxychloroquine, and interferon (IFN)- β 1a were discontinued for futility but randomisation to remdesivir continued. Here, we report the final results of Solidarity and meta-analyses of mortality in all relevant trials to date.

Methods: Solidarity enrolled consenting adults (aged ≥ 18 years) recently hospitalised with, in the view of their doctor, definite COVID-19 and no contraindication to any of the study drugs, regardless of any other patient characteristics. Participants were randomly allocated, in equal proportions between the locally available options, to receive whichever of the four study drugs (lopinavir, hydroxychloroquine, IFN- β 1a, or remdesivir) were locally available at that time or no study drug (controls). All patients also received the local standard of care. No placebos were given. The protocol-specified primary endpoint was in-hospital mortality, subdivided by disease severity. Secondary endpoints were progression to ventilation if not already ventilated, and time-to-discharge from hospital. Final log-rank and Kaplan-Meier analyses are presented for remdesivir, and are appended for all four study drugs. Meta-analyses give weighted averages of the mortality findings in this and all other randomised trials of these drugs among hospital inpatients. Solidarity is registered with ISRCTN, ISRCTN83971151, and ClinicalTrials.gov, NCT04315948.

Findings: Between March 22, 2020, and Jan 29, 2021, 14 304 potentially eligible patients were recruited from 454 hospitals in 35 countries in all six WHO regions. After the exclusion of 83 (0.6%) patients with a refuted COVID-19 diagnosis or encrypted consent not entered into the database, Solidarity enrolled 14 221 patients, including 8275 randomly allocated (1:1) either to remdesivir (ten daily infusions, unless discharged earlier) or to its control (allocated no study drug although remdesivir was locally available). Compliance was high in both groups. Overall, 602 (14.5%) of 4146 patients assigned to remdesivir died versus 643

(15.6%) of 4129 assigned to control (mortality rate ratio [RR] 0.91 [95% CI 0.82-1.02], $p=0.12$). Of those already ventilated, 151 (42.1%) of 359 assigned to remdesivir died versus 134 (38.6%) of 347 assigned to control (RR 1.13 [0.89-1.42], $p=0.32$). Of those not ventilated but on oxygen, 14.6% assigned to remdesivir died versus 16.3% assigned to control (RR 0.87 [0.76-0.99], $p=0.03$). Of 1730 not on oxygen initially, 2.9% assigned to remdesivir died versus 3.8% assigned to control (RR 0.76 [0.46-1.28], $p=0.30$). Combining all those not ventilated initially, 11.9% assigned to remdesivir died versus 13.5% assigned to control (RR 0.86 [0.76-0.98], $p=0.02$) and 14.1% versus 15.7% progressed to ventilation (RR 0.88 [0.77-1.00], $p=0.04$). The non-prespecified composite outcome of death or progression to ventilation occurred in 19.6% assigned to remdesivir versus 22.5% assigned to control (RR 0.84 [0.75-0.93], $p=0.001$). Allocation to daily remdesivir infusions (vs open-label control) delayed discharge by about 1 day during the 10-day treatment period. A meta-analysis of mortality in all randomised trials of remdesivir versus no remdesivir yielded similar findings.

Interpretation: Remdesivir has no significant effect on patients with COVID-19 who are already being ventilated. Among other hospitalised patients, it has a small effect against death or progression to ventilation (or both)."

Pre-Existing Conditions and Comorbidities

Journal Articles

JAMA Netw Open: [Differences in Outcomes and Factors Associated With Mortality Among Patients With SARS-CoV-2 Infection and Cancer Compared With Those Without Cancer: A Systematic Review and Meta-analysis](#) (09 May 2022)

"Question: What are the clinical outcomes for patients with both cancer and SARS-CoV-2 infection?

Findings: In this systematic review and meta-analysis of 81 studies involving 61 532 patients with cancer, patients who were younger, had lung cancer, or had hematologic cancer were at an increased risk of mortality from COVID-19. Among anticancer treatments, chemotherapy was associated with the highest mortality risk and endocrine therapy was associated with the lowest risk.

Meaning: Findings of this study suggest that younger patients with cancer are a high-risk population for poor outcomes from COVID-19."

Infect Dis Model: [Dynamics of novel COVID-19 in the presence of Co-morbidity](#) (04 May 2022)

"A novel coronavirus (COVID-19) has emerged as a global serious public health issue from December 2019. People having a weak immune system are more susceptible to coronavirus infection. It is a double challenge for people of any age with certain underlying medical conditions including cardiovascular disease, diabetes, high blood pressure and cancer etc. Co-morbidity increases the probability of COVID-19 complication. In this paper a deterministic compartmental model is formulated to understand the transmission dynamics of COVID-19. Rigorous mathematical analysis of the model shows that it exhibits backward bifurcation phenomenon when the basic reproduction number is less than unity. For the case of no re-infection it is shown that having the reproduction number less than one is necessary and sufficient for the effective control of COVID-19, that is, the disease free equilibrium is globally asymptotically stable when the reproduction threshold is less than unity. Furthermore, in the absence of reinfection, a unique endemic equilibrium of the model exists which is globally asymptotically stable whenever the reproduction number is greater than unity. Numerical simulations of the model, using data relevant to COVID-19 transmission dynamics, show that the use of efficacious face masks publicly could lead to the elimination of COVID-19 up to a satisfactory level. The study also shows that in the presence of co-morbidity, the disease increases significantly."

PLoS One: [Characterizing cancer and COVID-19 outcomes using electronic health records](#) (04 May 2022)

"Purpose: Patients with cancer often have compromised immune system which can lead to worse COVID-19 outcomes. The purpose of this study is to assess the association between COVID-19 outcomes and existing cancer-specific characteristics.

Patients and methods: Patients aged 18 or older with laboratory-confirmed COVID-19 between June 1, 2020, and December 31, 2020, were identified (n = 314 004) from the Optum® de-identified COVID-19 Electronic Health Record (EHR) derived from more than 700 hospitals and 7000 clinics in the United States. To allow sufficient observational time, patients with less than one year of medical history in the EHR dataset before their COVID-19 tests were excluded (n = 42 365). Assessed COVID-19 outcomes including all-cause 30-day mortality, hospitalization, ICU admission, and ventilator use, which were compared using relative risks (RRs) according to cancer status and treatments.

Results: Among 271 639 patients with COVID-19, 18 460 had at least one cancer diagnosis: 8034 with a history of cancer and 10 426 with newly diagnosed cancer within one year of COVID-19 infection. Patients with a cancer diagnosis were older and more likely to be male, white, Medicare beneficiaries, and have higher prevalences of chronic conditions. Cancer patients had higher risks for 30-day mortality (RR 1.07, 95% CI 1.01-1.14, P = 0.028) and hospitalization (RR 1.04, 95% CI 1.01-1.07, P = 0.006) but without significant differences in ICU admission and ventilator use compared to non-cancer patients. Recent cancer diagnoses were associated with higher risks for worse COVID-19 outcomes (RR for mortality

1.17, 95% CI 1.08-1.25, $P < 0.001$ and RR for hospitalization 1.10, 95% CI 1.06-1.14, $P < 0.001$), particularly among recent metastatic (stage IV), hematological, liver and lung cancers compared with the non-cancer group. Among COVID-19 patients with recent cancer diagnosis, mortality was associated with chemotherapy or radiation treatments within 3 months before COVID-19. Age, black patients, Medicare recipients, South geographic region, cardiovascular, diabetes, liver, and renal diseases were also associated with increased mortality.

Conclusions and relevance: Individuals with cancer had higher risks for 30-day mortality and hospitalization after SARS-CoV-2 infection compared to patients without cancer. More specifically, patients with a cancer diagnosis within 1 year and those receiving active treatment were more vulnerable to worse COVID-19 outcomes."

Long COVID and Other Post-Infectious Findings

News in Brief

"Scientists explore why some COVID long-haulers develop multiple health issues" ([NPR](#)).

"Coronavirus 'ghosts' found lingering in the gut: Scientists are studying whether long COVID could be linked to viral fragments found in the body months after initial infection" ([Nature](#)).

"Surviving the pandemic is only half the battle: 'Long COVID' could affect a billion in just a few years" ([Fortune](#)).

"Long Covid: Free online breathing course by opera singers can improve long-term symptoms, study finds" ([inews UK](#)).

Long Reads

"The promising treatment for long COVID we're not even trying: Early anecdotes about Paxlovid's effects on long COVID are intriguing, but no one's testing them in clinical trials yet" ([Atlantic](#)).

"Long COVID patients say doctors are ignoring their symptoms" ([BuzzFeed](#)).

Other Resources

Webinar (recorded May 2022): [Evaluating and Supporting Patients Presenting with Cognitive Symptoms Following COVID \(CDC\)](#)

The American Academy of Physical Medicine and Rehabilitation has a dashboard that estimates state and county level data and trends over time the millions of Americans affected by Post-Acute Sequelae of SARS-CoV-2 infection (PASC, aka Long COVID) ([AAPM&R PASC Dashboard](#)).

Preprints

[Long Covid: A Systematic Review and Meta-Analysis of 120,970 Patients](#)

[Effect of oral nirmatrelvir on Long COVID symptoms: a case series](#)

Special Reports and Other Resources

GAO: [Long COVID](#) (02 May 2022)

"How many people in the U.S. have developed "long COVID"?

It could be in the range of 7.7–23 million, some estimates say.

We discuss what is and isn't known about long COVID—new, returning, or ongoing health problems 4 or more weeks after an initial case of COVID-19. For example, some people with the condition experience chronic fatigue and have to stop working, which can affect their income and health insurance. But other economic effects are still unclear.

The federal government is taking steps to fund more research and help affected people. We describe challenges it could encounter and provide questions for policymakers to consider."

Journal Articles

Front Med: [The Impact of Initial COVID-19 Episode Inflammation Among Adults on Mortality Within 12 Months Post-hospital Discharge](#) (12 May 2022)

"Background: Inflammation in the initial COVID-19 episode may be associated with post-recovery mortality. The goal of this study was to determine the relationship between systemic inflammation in COVID-19 hospitalized adults and mortality after recovery from COVID-19.

Methods: An analysis of electronic health records (EHR) for patients from 1 January, 2020 through 31 December, 2021 was performed for a cohort of COVID-19 positive hospitalized adult patients. 1,207 patients were followed for 12 months post COVID-19 episode at one health system. 12-month risk of mortality associated with inflammation, C-reactive protein (CRP), was assessed in Cox regressions adjusted for age, sex, race and comorbidities. Analyses evaluated whether steroids prescribed upon discharge were associated with later mortality.

Results: Elevated CRP was associated with other indicators of severity of the COVID-19 hospitalization including, supplemental oxygen and intravenous dexamethasone. Elevated CRP was associated with an increased mortality risk after recovery from COVID-19. This effect was present for both unadjusted (HR = 1.60; 95% CI 1.18, 2.17) and adjusted analyses (HR = 1.61; 95% CI 1.19, 2.20) when CRP was split into high and low groups at the median. Oral steroid prescriptions at discharge were found to be associated with a lower risk of death post-discharge (adjusted HR = 0.49; 95% CI 0.33, 0.74).

Discussion: Hyperinflammation present with severe COVID-19 is associated with an increased mortality risk after hospital discharge. Although suggestive, treatment with anti-inflammatory medications like steroids upon hospital discharge is associated with a decreased post-acute COVID-19 mortality risk."

Lancet Respir Med: [Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study](#) (11 May 2022)

"Background: With the ongoing COVID-19 pandemic, growing evidence shows that a considerable proportion of people who have recovered from COVID-19 have long-term effects on multiple organs and systems. A few longitudinal studies have reported on the persistent health effects of COVID-19, but the follow-up was limited to 1 year after acute infection. The aim of our study was to characterise the longitudinal evolution of health outcomes in hospital survivors with different initial disease severity throughout 2 years after acute COVID-19 infection and to determine their recovery status.

Methods: We did an ambidirectional, longitudinal cohort study of individuals who had survived hospitalisation with COVID-19 and who had been discharged from Jin Yin-tan Hospital (Wuhan, China) between Jan 7 and May 29, 2020. We measured health outcomes 6 months (June 16–Sept 3, 2020), 12 months (Dec 16, 2020–Feb 7, 2021), and 2 years (Nov 16, 2021–Jan 10, 2022) after symptom onset with a 6-min walking distance (6MWD) test, laboratory tests, and a series of questionnaires on symptoms, mental health, health-related quality of life (HRQoL), return to work, and health-care use after discharge. A subset of COVID-19 survivors received pulmonary function tests and chest imaging at each visit. Age-matched, sex-matched, and comorbidities-matched participants without COVID-19 infection (controls) were introduced to determine the recovery status of COVID-19 survivors at 2 years. The primary outcomes included symptoms, modified British Medical Research Council (mMRC) dyspnoea scale, HRQoL, 6MWD, and return to work, and were assessed in all COVID-19 survivors who attended all three follow-up visits. Symptoms, mMRC dyspnoea scale, and HRQoL were also assessed in controls.

Findings: 2469 patients with COVID-19 were discharged from Jin Yin-tan Hospital between Jan 7 and May 29, 2020. 1192 COVID-19 survivors completed assessments at the three follow-up visits and were included in the final analysis, 1119 (94%) of whom attended the

face-to-face interview 2 years after infection. The median age at discharge was 57·0 years (48·0–65·0) and 551 (46%) were women. The median follow-up time after symptom onset was 185·0 days (IQR 175·0–197·0) for the visit at 6 months, 349·0 days (337·0–360·0) for the visit at 12 months, and 685·0 days (675·0–698·0) for the visit at 2 years. The proportion of COVID-19 survivors with at least one sequelae symptom decreased significantly from 777 (68%) of 1149 at 6 months to 650 (55%) of 1190 at 2 years ($p<0\cdot0001$), with fatigue or muscle weakness always being the most frequent. The proportion of COVID-19 survivors with an mMRC score of at least 1 was 168 (14%) of 1191 at 2 years, significantly lower than the 288 (26%) of 1104 at 6 months ($p<0\cdot0001$). HRQoL continued to improve in almost all domains, especially in terms of anxiety or depression: the proportion of individuals with symptoms of anxiety or depression decreased from 256 (23%) of 1105 at 6 months to 143 (12%) 1191 at 2 years ($p<0\cdot0001$). The proportion of individuals with a 6MWD less than the lower limit of the normal range declined continuously in COVID-19 survivors overall and in the three subgroups of varying initial disease severity. 438 (89%) of 494 COVID-19 survivors had returned to their original work at 2 years. Survivors with long COVID symptoms at 2 years had lower HRQoL, worse exercise capacity, more mental health abnormality, and increased health-care use after discharge than survivors without long COVID symptoms. COVID-19 survivors still had more prevalent symptoms and more problems in pain or discomfort, as well as anxiety or depression, at 2 years than did controls. Additionally, a significantly higher proportion of survivors who had received higher-level respiratory support during hospitalisation had lung diffusion impairment (43 [65%] of 66 vs 24 [36%] of 66, $p=0\cdot0009$), reduced residual volume (41 [62%] vs 13 [20%], $p<0\cdot0001$), and total lung capacity (26 [39%] vs four [6%], $p<0\cdot0001$) than did controls.

Interpretation: Regardless of initial disease severity, COVID-19 survivors had longitudinal improvements in physical and mental health, with most returning to their original work within 2 years; however, the burden of symptomatic sequelae remained fairly high. COVID-19 survivors had a remarkably lower health status than the general population at 2 years. The study findings indicate that there is an urgent need to explore the pathogenesis of long COVID and develop effective interventions to reduce the risk of long COVID."

Patient: [Long COVID Citizen Scientists: Developing a Needs-Based Research Agenda by Persons Affected by Long COVID](#) (28 April 2022)

"Background: Long-term health consequences following acute SARS-CoV-2 infection, referred to as post-COVID-19 condition or Long COVID, are increasing, with population-based prevalence estimates for adults at around 20%. Persons affected by Long COVID report various health problems, yet evidence to guide clinical decision making remains scarce.

Objective: The present study aimed to identify Long COVID research priorities using a citizen science approach and solely considering the needs of those affected.

Methods: This citizen science study followed an iterative process of patient needs identification, evaluation and prioritisation. A Long COVID Citizen Science Board (21 persons with Long COVID, and seven with myalgic encephalomyelitis/chronic fatigue syndrome) and a Long COVID Working Group (25 persons with Long COVID, four patients with myalgic encephalomyelitis/chronic fatigue syndrome and one relative) were formed. The study included four activities: three remote meetings and one online survey. First, Board members identified the needs and research questions. Second, Working Group members and persons affected by Long COVID (241 respondents, 85.5% with Long COVID, 14.5% with myalgic encephalomyelitis/chronic fatigue syndrome and 7.1% relatives) evaluated the research questions on a 1-5 Likert scale using an online survey. Then the Board gave feedback on this evaluation. Finally, Board members set the priorities for research through voting and discussion.

Results: Sixty-eight research questions were generated by the Board and categorised into four research domains (medicine, healthcare services, socioeconomics and burden of disease) and 14 subcategories. Their average importance ratings were moderate to high and varied from 3.41 (standard deviation = 1.16) for sex-specific diagnostics to 4.86 (standard deviation = 0.41) for medical questions on treatment. Five topics were prioritised: "treatment, rehabilitation and chronic care management", "availability of interfaces for treatment continuity", "availability of healthcare structures", "awareness and knowledge among professionals" and "prevalence of Long COVID in children and adolescents".

Conclusions: To our knowledge, this is the first study developing a citizen-driven, explicitly patient-centred research agenda with persons affected by Long COVID, setting it apart from existing multi-stakeholder efforts. The identified priorities could guide future research and funding allocation. Our methodology establishes a framework for citizen-driven research agendas, suitable for transfer to other diseases."

Crit Care Explor: [Neurologic Manifestations of Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Hospitalized Patients During the First Year of the COVID-19 Pandemic](#) (25 April 2022)

"OBJECTIVES: To describe the prevalence, associated risk factors, and outcomes of serious neurologic manifestations (encephalopathy, stroke, seizure, and meningitis/encephalitis) among patients hospitalized with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

DESIGN: Prospective observational study.

SETTING: One hundred seventy-nine hospitals in 24 countries within the Society of Critical Care Medicine Discovery Viral Infection and Respiratory Illness Universal Study COVID-19 Registry.

PATIENTS: Hospitalized adults with laboratory-confirmed SARS-CoV-2 infection.

INTERVENTIONS: None.

RESULTS: Of 16,225 patients enrolled in the registry with hospital discharge status available, 2,092 (12.9%) developed serious neurologic manifestations including 1,656 (10.2%) with encephalopathy at admission, 331 (2.0%) with stroke, 243 (1.5%) with seizure, and 73 (0.5%) with meningitis/encephalitis at admission or during hospitalization. Patients with serious neurologic manifestations of COVID-19 were older with median (interquartile range) age 72 years (61.0–81.0 yr) versus 61 years (48.0–72.0 yr) and had higher prevalence of chronic medical conditions, including vascular risk factors. Adjusting for age, sex, and time since the onset of the pandemic, serious neurologic manifestations were associated with more severe disease (odds ratio [OR], 1.49; $p < 0.001$) as defined by the World Health Organization ordinal disease severity scale for COVID-19 infection. Patients with neurologic manifestations were more likely to be admitted to the ICU (OR, 1.45; $p < 0.001$) and require critical care interventions (extracorporeal membrane oxygenation: OR, 1.78; $p = 0.009$ and renal replacement therapy: OR, 1.99; $p < 0.001$). Hospital, ICU, and 28-day mortality for patients with neurologic manifestations was higher (OR, 1.51, 1.37, and 1.58; $p < 0.001$), and patients had fewer ICU-free, hospital-free, and ventilator-free days (estimated difference in days, -0.84 , -1.34 , and -0.84 ; $p < 0.001$).

CONCLUSIONS: Encephalopathy at admission is common in hospitalized patients with SARS-CoV-2 infection and is associated with worse outcomes. While serious neurologic manifestations including stroke, seizure, and meningitis/encephalitis were less common, all were associated with increased ICU support utilization, more severe disease, and worse outcomes."

Lancet Respir Med: [Clinical characteristics with inflammation profiling of long COVID and association with 1-year recovery following hospitalisation in the UK: a prospective observational study](#) (23 April 2022)

"Background: No effective pharmacological or non-pharmacological interventions exist for patients with long COVID. We aimed to describe recovery 1 year after hospital discharge for COVID-19, identify factors associated with patient-perceived recovery, and identify potential therapeutic targets by describing the underlying inflammatory profiles of the previously described recovery clusters at 5 months after hospital discharge.

Methods: The Post-hospitalisation COVID-19 study (PHOSP-COVID) is a prospective, longitudinal cohort study recruiting adults (aged ≥ 18 years) discharged from hospital with COVID-19 across the UK. Recovery was assessed using patient-reported outcome measures, physical performance, and organ function at 5 months and 1 year after hospital discharge, and stratified by both patient-perceived recovery and recovery cluster. Hierarchical logistic regression modelling was performed for patient-perceived recovery at 1 year. Cluster

analysis was done using the clustering large applications k-medoids approach using clinical outcomes at 5 months. Inflammatory protein profiling was analysed from plasma at the 5-month visit. This study is registered on the ISRCTN Registry, ISRCTN10980107, and recruitment is ongoing.

Findings: 2320 participants discharged from hospital between March 7, 2020, and April 18, 2021, were assessed at 5 months after discharge and 807 (32.7%) participants completed both the 5-month and 1-year visits. 279 (35.6%) of these 807 patients were women and 505 (64.4%) were men, with a mean age of 58.7 (SD 12.5) years, and 224 (27.8%) had received invasive mechanical ventilation (WHO class 7-9). The proportion of patients reporting full recovery was unchanged between 5 months (501 [25.5%] of 1965) and 1 year (232 [28.9%] of 804). Factors associated with being less likely to report full recovery at 1 year were female sex (odds ratio 0.68 [95% CI 0.46-0.99]), obesity (0.50 [0.34-0.74]) and invasive mechanical ventilation (0.42 [0.23-0.76]). Cluster analysis (n=1636) corroborated the previously reported four clusters: very severe, severe, moderate with cognitive impairment, and mild, relating to the severity of physical health, mental health, and cognitive impairment at 5 months. We found increased inflammatory mediators of tissue damage and repair in both the very severe and the moderate with cognitive impairment clusters compared with the mild cluster, including IL-6 concentration, which was increased in both comparisons (n=626 participants). We found a substantial deficit in median EQ-5D-5L utility index from before COVID-19 (retrospective assessment; 0.88 [IQR 0.74-1.00]), at 5 months (0.74 [0.64-0.88]) to 1 year (0.75 [0.62-0.88]), with minimal improvements across all outcome measures at 1 year after discharge in the whole cohort and within each of the four clusters.

Interpretation: The sequelae of a hospital admission with COVID-19 were substantial 1 year after discharge across a range of health domains, with the minority in our cohort feeling fully recovered. Patient-perceived health-related quality of life was reduced at 1 year compared with before hospital admission. Systematic inflammation and obesity are potential treatable traits that warrant further investigation in clinical trials."

Eur J Neurol: [Short- and long-term outcome and predictors in an international cohort of patients with neuro-COVID-19](#) (online 23 February 2022)

"Background and purpose: Despite the increasing number of reports on the spectrum of neurological manifestations of COVID-19 (neuro-COVID), few studies have assessed short- and long-term outcome of the disease.

Methods: This is a cohort study enrolling adult patients with neuro-COVID seen in neurological consultation. Data were collected prospectively or retrospectively in the European Academy of Neurology NEuro-covid ReGistrY ((ENERGY). The outcome at discharge was measured using the modified Rankin Scale and defined as 'stable/improved' if

the modified Rankin Scale score was equal to or lower than the pre-morbid score, 'worse' if the score was higher than the pre-morbid score. Status at 6 months was also recorded. Demographic and clinical variables were assessed as predictors of outcome at discharge and 6 months.

Results: From July 2020 to March 2021, 971 patients from 19 countries were included. 810 (83.4%) were hospitalized. 432 (53.3%) were discharged with worse functional status. Older age, stupor/coma, stroke and intensive care unit (ICU) admission were predictors of worse outcome at discharge. 132 (16.3%) died in hospital. Older age, cancer, cardiovascular complications, refractory shock, stupor/coma and ICU admission were associated with death. 262 were followed for 6 months. Acute stroke or ataxia, ICU admission and degree of functional impairment at discharge were predictors of worse outcome. 65/221 hospitalized patients (29.4%) and 10/32 non-hospitalized patients (24.4%) experienced persisting neurological symptoms/signs. 10/262 patients (3.8%) developed new neurological complaints during the 6 months of follow-up.

Conclusions: Neuro-COVID is a severe disease associated with worse functional status at discharge, particularly in older subjects and those with comorbidities and acute complications of infection."

Pregnancy and Postpartum Period

News in Brief

"Overturn of Roe could make IVF more complicated, costly" ([WP](#)).

Journal Articles

Lancet Reg Health Am: [Maternal mortality linked to COVID-19 in Latin America: Results from a multi-country collaborative database of 447 deaths](#) (06 May 2022)

"Background: This study aimed to describe the clinical characteristics of maternal deaths associated with COVID-19 registered in a collaborative Latin-American multi-country database.

Methods: This was an observational study implemented from March 1st 2020 to November 29th 2021 in eight Latin American countries. Information was based on the Perinatal Information System from the Latin American Center for Perinatology, Women and Reproductive Health. We summarized categorical variables as frequencies and percentages and continuous variables into median with interquartile ranges.

Findings: We identified a total of 447 deaths. The median maternal age was 31 years. 86.4% of women were infected antepartum, with most of the cases (60.3%) detected in the third trimester of pregnancy. The most frequent symptoms at first consultation and admission were dyspnea (73.0%), fever (69.0%), and cough (59.0%). Organ dysfunction was reported in 90.4% of women during admission. A total of 64.8% women were admitted to critical care for a median length of eight days. In most cases, the death occurred during the puerperium, with a median of seven days between delivery and death. Preterm delivery was the most common perinatal complication (76.9%) and 59.9% were low birth weight.

Interpretation: This study describes the characteristics of maternal deaths in a comprehensive multi-country database in Latin America during the COVID-19 pandemic. Barriers faced by Latin American pregnant women to access intensive care services when required were also revealed. Decision-makers should strengthen severity awareness, and referral strategies to avoid potential delays."

Obstet Gynecol: [Neighborhood Characteristics and Racial Disparities in Severe Acute Respiratory Syndrome Coronavirus 2 \(SARS-CoV-2\) Seropositivity in Pregnancy](#) (05 May 2022)

"OBJECTIVE: To quantify the extent to which neighborhood characteristics contribute to racial and ethnic disparities in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seropositivity in pregnancy.

METHODS: This cohort study included pregnant patients who presented for childbirth at two hospitals in Philadelphia, Pennsylvania from April 13 to December 31, 2020. Seropositivity for SARS-CoV-2 was determined by measuring immunoglobulin G and immunoglobulin M antibodies by enzyme-linked immunosorbent assay in discarded maternal serum samples obtained for clinical purposes. Race and ethnicity were self-reported and abstracted from medical records. Patients' residential addresses were geocoded to obtain three Census tract variables: community deprivation, racial segregation (Index of Concentration at the Extremes), and crowding. Multivariable mixed effects logistic regression models and causal mediation analyses were used to quantify the extent to which neighborhood variables may explain racial and ethnic disparities in seropositivity.

RESULTS: Among 5,991 pregnant patients, 562 (9.4%) were seropositive for SARS-CoV-2. Higher seropositivity rates were observed among Hispanic (19.3%, 104/538) and Black (14.0%, 373/2,658) patients, compared with Asian (3.2%, 13/406) patients, White (2.7%, 57/2,133) patients, and patients of another race or ethnicity (5.9%, 15/256) ($P < .001$). In adjusted models, per SD increase, deprivation (adjusted odds ratio [aOR] 1.16, 95% CI 1.02–1.32) and crowding (aOR 1.15, 95% CI 1.05–1.26) were associated with seropositivity, but segregation was not (aOR 0.90, 95% CI 0.78–1.04). Mediation analyses revealed that crowded housing may explain 6.7% (95% CI 2.0–14.7%) of the Hispanic–White disparity and

that neighborhood deprivation may explain 10.2% (95% CI 0.5–21.1%) of the Black–White disparity.

CONCLUSION: Neighborhood deprivation and crowding were associated with SARS-CoV-2 seropositivity in pregnancy in the prevaccination era and may partially explain high rates of SARS-CoV-2 seropositivity among Black and Hispanic patients. Investing in structural neighborhood improvements may reduce inequities in viral transmission."

JAMA: [Association of SARS-CoV-2 Infection During Pregnancy With Maternal and Perinatal Outcomes](#) (02 May 2022)

"Question: Is SARS-CoV-2 infection during pregnancy associated with increased risk of adverse maternal and perinatal outcomes?

Findings: This Canadian surveillance study included 6012 completed pregnancies between March 2020 and October 2021. Among cases of infection during pregnancy compared with cases of infection among the general Canadian population of reproductive-age female individuals, there was a significantly increased risk of SARS-CoV-2–related hospitalization (relative risk, 2.65) and intensive care unit admission (relative risk, 5.46). Among cases of infection during pregnancy compared with pregnant individuals without SARS-CoV-2 infection, there was a significantly increased risk of preterm birth (relative risk, 1.63).

Meaning: SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth."

Pediatric Population

News in Brief

"Moderna completes FDA submission for use of COVID shot in adolescents, kids" ([Reuters](#)).

"Most US kids have caught the coronavirus, antibody survey finds" ([Nature](#); see also: [SSRN preprint](#)).

"Kids get limited COVID protection from world's most popular vaccines: First analyses of two Chinese-made vaccines in young children show that the shots do provide 60–65% effectiveness against hospitalization" ([Nature](#)).

"Children get long Covid, too, and it can show up in unexpected ways" ([CNN](#)).

"1M U.S. COVID deaths mean pandemic orphan numbers reach 250,000: David Muir Reports" ([ABC](#)).

Beyond COVID

"Unexplained hepatitis cases in kids rise to 348 in 20 nations" ([CIDRAP](#)).

"With usual suspects ruled out, disease detectives try to crack mystery of viral hepatitis cases in kids" ([STAT](#)).

"The Alabama doc who sounded the alarm on unusual hepatitis in kids" ([Medpage](#)).

MMWR: [Acute Hepatitis and Adenovirus Infection Among Children — Alabama, October 2021–February 2022](#) (06 May 2022)

Journal Articles

NEJM: [Evaluation of mRNA-1273 Covid-19 Vaccine in Children 6 to 11 Years of Age](#) (11 May 2022)

"Background: Vaccination of children to prevent coronavirus disease 2019 (Covid-19) is an urgent public health need. The safety, immunogenicity, and efficacy of the mRNA-1273 vaccine in children 6 to 11 years of age are unknown.

Methods: Part 1 of this ongoing phase 2-3 trial was open label for dose selection; part 2 was an observer-blinded, placebo-controlled expansion evaluation of the selected dose. In part 2, we randomly assigned children (6 to 11 years of age) in a 3:1 ratio to receive two injections of mRNA-1273 (50 µg each) or placebo, administered 28 days apart. The primary objectives were evaluation of the safety of the vaccine in children and the noninferiority of the immune response in these children to that in young adults (18 to 25 years of age) in a related phase 3 trial. Secondary objectives included determination of the incidences of confirmed Covid-19 and severe acute respiratory syndrome coronavirus 2 infection, regardless of symptoms. Interim analysis results are reported.

Results: In part 1 of the trial, 751 children received 50-µg or 100-µg injections of the mRNA-1273 vaccine, and on the basis of safety and immunogenicity results, the 50-µg dose level was selected for part 2. In part 2 of the trial, 4016 children were randomly assigned to receive two injections of mRNA-1273 (50 µg each) or placebo and were followed for a median of 82 days (interquartile range, 14 to 94) after the first injection. This dose level was associated with mainly low-grade, transient adverse events, most commonly injection-site pain, headache, and fatigue. No vaccine-related serious adverse events, multisystem inflammatory syndrome in children, myocarditis, or pericarditis were reported as of the data-cutoff date. One month after the second injection (day 57), the neutralizing antibody titer in children who received mRNA-1273 at a 50-µg level was 1610 (95% confidence interval [CI], 1457 to 1780), as compared with 1300 (95% CI, 1171 to 1443) at the 100-µg level in young adults, with serologic responses in at least 99.0% of the participants in both

age groups, findings that met the prespecified noninferiority success criterion. Estimated vaccine efficacy was 88.0% (95% CI, 70.0 to 95.8) against Covid-19 occurring 14 days or more after the first injection, at a time when B.1.617.2 (delta) was the dominant circulating variant.

Conclusions: Two 50-µg doses of the mRNA-1273 vaccine were found to be safe and effective in inducing immune responses and preventing Covid-19 in children 6 to 11 years of age; these responses were noninferior to those in young adults."

Psychol Rep: [Social and Psychological Effects of COVID-19 Pandemic on Adolescents' and Young Adults' Mental Health: A Cross-Cultural Mediation Study](#) (09 May 2022)

"The ongoing pandemic has dramatically disrupted daily life, increasing the risk of developing psychiatric disorders and poor mental wellbeing. The compound effects of social, political and psychological stressors have increased psychological symptoms among adolescents and young people, with worries about COVID-19 playing a central role in the clinical course of their mental health problems caused by the pandemic. The aim of this cross-cultural study was to examine the social psychological effects of COVID-19 on adolescents' and young people's mental health and wellbeing in Ibero-American population. Participants involved 6,283 adolescents and young adults from five different Spanish-Speaking countries (83.7% female) aged between 12 and 30 years (M = 18.79; SD = 3.48). Participants completed the Worries about COVID-19 and its Consequences Scale (W-COV), the Satisfaction with Life Scale (SWLS), and the Depression, Anxiety and Stress Scale (DASS-21). Descriptive analyses, multivariate ANOVAs and Pearson correlations were performed, as well as Structural Equation Modelling (SEM) testing a mediational model. The results indicate cross-cultural difference in COVID-19 related worries, emotional symptoms and life satisfaction. Results from SEM confirmed the overall indirect effects of COVID-19 cases, political response and participants' conditions during lockdown on depression, anxiety, stress and life satisfaction mediated by COVID-19 related worries. These findings suggest that the social psychological factors underlying psychological symptoms could be partly explained by increased worries about COVID-19 and its personal, social, economic and political consequences, which may offer guidance to policy makers and health services for safeguarding youth mental well-being."

Ann Med Surg (Lond): [Observational study on necrotizing enterocolitis in neonates born to SARS-CoV-2-positive mothers](#) (06 May 2022)

"Background: The impact of the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) pandemic on expectant mother and their babies extends to many aspects of life. Necrotizing enterocolitis (NEC) has been recognized as a life-threatening gastrointestinal inflammatory process in neonates that has high rates of morbidity and mortality.

Objective: To investigate factors associated with NEC in hospitalized neonates whose mothers were SARS-CoV-2-positive and their relationship to mortality.

Method: This observational study was conducted from May 2020 to March 2021. All neonates who were hospitalized, after confirming that the mother was SARS-CoV-2-positive, were included in this study. The confirmation of positive SARS-CoV-2 was determined according to the reverse transcription-polymerase chain reaction (PCR) assay. The neonatal SARS-CoV-2 test was performed on the first day of birth. NEC was established based on a suggestive clinical presentation and abnormal abdominal radiographs.

Results: Of the 125 neonates enrolled in this study, there were 5 neonates who developed NEC and only one survived. Significant associated factors with NEC included lower birth weight ($p < 0.001$), lower gestational age ($p < 0.001$), positive SARS-CoV-2 PCR results (OR = 15.333; 95% CI = 2.074-113.381, $p = 0.007$), asphyxia (OR = 13.143; 95% CI = 1.411-122.443, $p = 0.024$), and mortality (OR = 156.000; 95% CI = 13.157-1849.623; $p < 0.001$). Mortality was significantly associated with lower gestational age ($p = 0.025$), cesarean section delivery ($p = 0.025$), and asphyxia ($p = 0.025$).

Conclusion: Significant associated factors with NEC in neonates born to SARS-CoV-2-positive mothers included positive SARS-CoV-2 PCR results, asphyxia, lower gestational age, and lower birth weight. In addition to caesarean section delivery, these factors were related to mortality in neonates in such conditions."

Neonatology: [Multisystemic Inflammatory Syndrome in Neonates: A Systematic Review](#) (05 May 2022)

"Introduction: Multisystem inflammatory syndrome in neonates (MIS-N) related to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has increasingly been reported worldwide amid the spread of the SARS-CoV-2 pandemic.

Methods: We searched PubMed, EMBASE, and CINAHL and preprint servers (BioRxiv.org and MedRxiv.org) using a specified strategy integrating Medical Subject Headings terms and keywords until October 20, 2021. Our aim was to systematically review demographic profiles, clinical features, laboratory parameters, complications, treatments, and outcomes of neonates with MIS-N. Studies were selected when fulfilling the inclusion criteria. Articles were included if they fulfilled the World Health Organization (WHO), Centers for Disease Control (CDC) definitions of MIS-C, or our proposed definition.

Results: Sixteen reports of MIS-N including 47 neonates meeting MIS-N criteria were identified. Presentation included cardiovascular compromise (77%), respiratory involvement (55%), and fever in (36%). Eighty-three percent of patients received steroids, and 76% received immunoglobulin. Respiratory support was provided to 60% of patients and inotropes to 45% of patients. Five (11%) neonates died.

Conclusion: The common presentation of MIS-N included cardiorespiratory compromise with the possibility of high mortality. Neonates with MIS-N related to SARS-CoV-2 may be at higher risk of adverse outcomes."

Healthcare Workers

News in Brief

"Doctors Without Borders addresses charges of racism within its ranks" ([NPR](#)).

Journal Articles

Acad Emerg Med: [The perceived work environment and well-being-a survey of emergency healthcare workers during the COVID-19 pandemic](#) (09 May 2022)

"Background: During the COVID-19 pandemic, health care provider well-being has been affected by various challenges in the work environment. The purpose of this study was to evaluate the relationship between the perceived work environment and mental well-being of a sample of emergency medicine (EM) physicians, EM nurses and emergency medical services (EMS) providers during the pandemic.

Methods: We surveyed EM attending physicians, EM resident physicians, EM nurses and emergency medical service providers from 10 academic sites across the United States. We used latent class analysis (LCA) to estimate the effect of the perceived work environment on screening positive for depression/anxiety and burnout controlling for respondent characteristics. We tested possible predictors in the multivariate regression models and included the predictors that were significant in the final model.

Results: Our final sample included 701 emergency health care workers. Almost 23% of respondents screened positive for depression/anxiety and 39.7% for burnout. Nurses were significantly more likely to screen positive for depression/anxiety (aOR=2.04: 95% CI 1.11, 3.86) and burnout (aOR=2.05: 95% CI 1.22, 3.49) compared to attendings. The LCA analysis identified 4 subgroups of our respondents that differed in their responses to the work environment questions. These groups were identified as: Work environment risk group 1, an overall good work environment; risk group 2, inadequate resources; risk group 3, lack of perceived organizational support and risk group 4, an overall poor work environment. Participants in the 2 groups who perceived their work conditions as most adverse were significantly more likely to screen positive for depression/anxiety (aOR=1.89: 95% CI 1.05,

3.42 and aOR=2.04: 95% CI 1.14, 3.66) compared to participants working in environments perceived as less adverse.

Conclusions: We found a strong association between a perceived adverse working environment and poor mental health, particularly when organizational support was deemed inadequate. Targeted strategies to promote better perceptions of the workplace are needed."

PLoS One: [Healthcare worker trauma and related mental health outcomes during the COVID-19 outbreak in New York City](#) (29 April 2022)

"Healthcare workers (HCWs) faced a range of stressors during the coronavirus (COVID-19) pandemic, contributing to psychological stress. We use a psychological trauma framework to characterize the mental health burden for clinical and non-clinical healthcare worker occupations during the COVID-19 pandemic. The objective was to measure and characterize risk factors for trauma and anxiety-related mental health problems among HCWs at a public hospital in the epicenter of the COVID-19 pandemic in New York City (NYC).

This study reports findings from a cross-sectional survey of NYC HCWs shortly after the initial 2020 infection surge. Over 800 hospital employees completed the survey that assessed professional quality of life indicators (compassion satisfaction [CS], burnout [BO], secondary traumatic stress [STS]), Coronavirus Anxiety (CS), Obsession with Coronavirus (OC), and PTSD symptoms. The survey also assessed pandemic-related work and life circumstances such as "do you have a family member or friend who tested positive for COVID". Relatively small percentages of HCWs endorsed probable Coronavirus Anxiety (6%), PTSD (13%), and Coronavirus Obsession (21%).

We observed higher proportions of Burnout (29%), Moderate or High Secondary Traumatic Stress (45%), and High Compassion Satisfaction (52%). Adjusted regression models showed important implications for prior behavioral/emotional health concerns among HCWs, providing care for a patient that died from COVID-19, and other characteristics.

This study supports prior studies documenting the mental health consequences for the healthcare workforce during the COVID-19 pandemic. This study builds on that base by including non-clinical staff in the sample and assessing pandemic life-stressors such as caring for sick family members."

Mental Health and Wellness

News in Brief

"Former US mental-health tsar calls for a care overhaul" ([Nature](#)).

"U.S. surpasses record 100,000 overdose deaths in 2021" ([WP](#)).

Journal Articles

JAMA Psychiatry: [Neuropsychiatric Ramifications of Severe COVID-19 and Other Severe Acute Respiratory Infections](#) (11 May 2022)

Note: includes audio of author interview

"Question: What are the risks of neuropsychiatric disorders in adults surviving COVID-19 hospitalization, and how do these compare with non-COVID severe respiratory infections?

Findings: In this cohort study of data from more than 8 million adults in England, during the COVID-19 pandemic, risks of new anxiety disorder, dementia, psychotic disorder, and bipolar disorder diagnoses were significantly increased in adults surviving hospitalization for COVID-19 or other severe acute respiratory infections compared with the general population. Risks of neuropsychiatric illnesses or commencement of related medications were similar for COVID-19 and non-COVID severe respiratory infections.

Meaning: The results of this study suggest that disease severity, rather than pathogen, is a relevant factor associated with neuropsychiatric ramifications after severe respiratory infections."

Alcohol Clin Exp Res: [Alcohol use trajectories among U.S. adults during the first 42 weeks of the COVID-19 pandemic](#) (09 May 2022)

"Background: This study characterized the prevalence, drinking patterns, and sociodemographic characteristics of U.S. adult subpopulations with distinct drinking trajectories during the COVID-19 pandemic's first 42 weeks.

Methods: Adult respondents (n = 8130) in a nationally representative prospective longitudinal study completed 21 biweekly web surveys (March 2020 to January 2021). Past-week alcohol drinking frequency (drinking days [range: 0 to 7]) and intensity (binge drinking on usual past-week drinking day [yes/no]) were assessed at each timepoint. Growth mixture models identified multiple subpopulations with homogenous drinking trajectories based on mean drinking days or binge drinking proportional probabilities across time.

Results: Four drinking frequency trajectories were identified: Minimal/stable (72.8% [95% CI = 71.8 to 73.8]) with <1 mean past-week drinking days throughout; Moderate/late

decreasing (6.7% [95% CI = 6.2 to 7.3]) with 3.13 mean March drinking days and reductions during summer, reaching 2.12 days by January 2021; Moderate/early increasing (12.9% [95% CI = 12.2 to 13.6]) with 2.13 mean March drinking days that increased in April and then plateaued, ending with 3.20 mean days in January 2021; and Near daily/early increasing (7.6% [95% CI = 7.0 to 8.2]) with 5.58 mean March drinking days that continued increasing without returning to baseline. Four drinking intensity trajectories were identified: Minimal/stable (85.8% [95% CI = 85.0% to 86.5%]) with <0.01 binge drinking probabilities throughout; Low-to-moderate/fluctuating (7.4% [95% CI = 6.8% to 8%]) with varying binge probabilities across timepoints (range:0.12 to 0.26); Moderate/mid increasing (4.2% [95% CI = 3.7% to 4.6%]) with 0.39 April binge drinking probability rising to 0.65 during August-September without returning to baseline; High/early increasing trajectory (2.7% [95% CI = 2.3% to 3%]) with 0.84 binge drinking probability rising to 0.96 by June without returning to baseline. Males, Whites, middle-aged/older adults, college degree recipients, those consistently working, and those above the poverty limit were overrepresented in various increasing (vs. minimal/stable) frequency trajectories. Males, Whites, nonmarried, those without college degree, 18 to 39-year-olds, and middle aged were overrepresented in increasing (vs. minimal/stable) intensity trajectories.

Conclusions: Several distinct U.S. adult sociodemographic subpopulations appear to have acquired new drinking patterns during the pandemic's first 42 weeks. Frequent alcohol use assessment in the COVID-19 era could improve personalized medicine and population health efforts to reduce drinking."

Am Psychol: [Loneliness before and during the COVID-19 pandemic: A systematic review with meta-analysis](#) (09 May 2022)

"The COVID-19 pandemic and measures aimed at its mitigation, such as physical distancing, have been discussed as risk factors for loneliness, which increases the risk of premature mortality and mental and physical health conditions. To ascertain whether loneliness has increased since the start of the pandemic, this study aimed to narratively and statistically synthesize relevant high-quality primary studies. This systematic review with meta-analysis was registered at PROSPERO (ID CRD42021246771). Searched databases were PubMed, PsycINFO, Cochrane Library/Central Register of Controlled Trials/EMBASE/CINAHL, Web of Science, the World Health Organization (WHO) COVID-19 database, supplemented by Google Scholar and citation searching (cutoff date of the systematic search December 5, 2021). Summary data from prospective research including loneliness assessments before and during the pandemic were extracted. Of 6,850 retrieved records, 34 studies (23 longitudinal, 9 pseudolongitudinal, 2 reporting both designs) on 215,026 participants were included. Risk of bias (RoB) was estimated using the risk of bias in non-randomised studies-of interventions (ROBINS-I) tool. Standardized mean differences (SMD, Hedges' g) for continuous loneliness values and logOR for loneliness prevalence rates were calculated as

pooled effect size estimators in random-effects meta-analyses. Pooling studies with longitudinal designs only (overall N = 45,734), loneliness scores (19 studies, SMD = 0.27 [95% confidence interval = 0.14-0.40], Z = 4.02, p < .001, I² = 98%) and prevalence rates (8 studies, logOR = 0.33 [0.04-0.62], Z = 2.25, p = .02, I² = 96%) increased relative to prepandemic times with small effect sizes. Results were robust with respect to studies' overall RoB, pseudolongitudinal designs, timing of prepandemic assessments, and clinical populations. The heterogeneity of effects indicates a need to further investigate risk and protective factors as the pandemic progresses to inform targeted interventions."

J Int Med Res: [Care models for mental health in a population of patients affected by COVID-19](#) (08 May 2022)

"Objective: Emergency psychological interventions are needed in patients with COVID-19. During the pandemic, psychological counseling services have been provided using online platforms to address adverse psychological impacts and symptoms in patients and the general population. We investigated the effects of telepsychotherapy on emotional well-being and psychological distress in patients affected by COVID-19.

Methods: Forty-five Sicilian patients who had contracted COVID-19 joined "Telecovid Sicilia" from March to June 2020. Participants completed self-assessment questionnaires and psychological testing to measure levels of anxiety, presence of depressive symptoms, and altered circadian rhythm with consequent sleep disorders and psychological distress. Individual telepsychotherapy services were provided for 1 hour, twice a week, for 16 sessions in total.

Results: We enrolled 45 patients (42.2% women). We found significant changes between baseline and the end of follow-up in all outcome measures, especially depression (χ^2 (1) = 30.1; effect size [ES] = 0.82), anxiety (χ^2 (1) = 37.4; ES = 0.91), and paranoid ideation (χ^2 (1) = 5.6; ES = 0.35). The proportion of participants with sleep disorders decreased to 84.1% after intervention (χ^2 (1) = 58.6; ES = 1.14).

Conclusion: A telepsychotherapeutic approach showed promising effects on psychological symptoms, with significantly reduced patient anxiety and depression."

Psychiatry Res: [Psychiatric disorders newly diagnosed among veterans subsequent to hospitalization for COVID-19](#) (22 April 2022)

"Objective: The goal of our study was to evaluate the development of new mental health diagnoses up to 6-months following COVID-19 hospitalization for in a large, national sample.

Method: Data were extracted for all Veterans hospitalized at Veterans Health Administration hospitals for COVID-19 from March through August of 2020 utilizing national administrative data. After identifying the cohort, follow-up data were linked through six months post-hospitalization. Data were analyzed using logistic regression.

Results: Eight percent of patients developed a new mental health diagnosis following hospitalization. The most common new mental health diagnoses involved depressive, anxiety, and adjustment disorders. Younger and rural patients were more likely to develop new mental health diagnoses. Women and those with more comorbidities were less likely to develop new diagnoses.

Conclusion: A subpopulation of patients hospitalized for COVID-19 developed new mental health diagnoses. Unique demographics predictors indicate the potential need for additional outreach and screening to groups at elevated risk of post-hospitalization, mental health sequelae."

Other Infectious Diseases and Public Health Threats

News in Brief

"Third Ebola case confirmed in northwest Congo, WHO says" ([Reuters](#)).

"How a COVID misdiagnosis revealed deadly aromatherapy outbreak" ([Medpage](#); see also: [NEJM article](#)).

"H5N1 avian flu now affecting more than two thirds of states" ([CIDRAP](#)).

"Ticks are spreading in the US—and taking new diseases with them" ([Wired](#)).

"How COVID vaccines have boosted the development of an HIV vaccine" ([NPR](#)).

"NIH launches clinical trial of Epstein-Barr virus vaccine" ([NIH](#)).

Journal Articles

MMWR: [Progress Toward Polio Eradication — Worldwide, January 2020–April 2022](#) (13 May 2022)

"What is already known about this topic? Wild poliovirus type 1 (WPV1) transmission remains endemic in Afghanistan and Pakistan. Outbreaks of paralysis due to circulating vaccine-derived polioviruses (cVDPVs) occur in populations with low immunity following prolonged circulation of Sabin strain oral poliovirus vaccine.

What is added by this report? In 2021, Afghanistan and Pakistan reported a sharp decline in WPV1 cases from previous years. A WPV1 case genetically linked to these countries occurred in Malawi in November 2021.

What are the implications for public health practice? Current progress toward polio eradication must be sustained in countries experiencing endemic transmission and outbreaks. Intensified programmatic actions leading to more effective outbreak responses and enhanced efforts to immunize all children are essential. Until WPV1 is eradicated and cVDPV transmission is interrupted, the risk for children being paralyzed by polio remains."

Nat Commun: [Archival influenza virus genomes from Europe reveal genomic variability during the 1918 pandemic](#) (10 May 2022)

"The 1918 influenza pandemic was the deadliest respiratory pandemic of the 20th century and determined the genomic make-up of subsequent human influenza A viruses (IAV). Here, we analyze both the first 1918 IAV genomes from Europe and the first from samples prior to the autumn peak. 1918 IAV genomic diversity is consistent with a combination of local transmission and long-distance dispersal events. Comparison of genomes before and during the pandemic peak shows variation at two sites in the nucleoprotein gene associated with resistance to host antiviral response, pointing at a possible adaptation of 1918 IAV to humans. Finally, local molecular clock modeling suggests a pure pandemic descent of seasonal H1N1 IAV as an alternative to the hypothesis of origination through an intrasubtype reassortment."

MMWR: [West Nile Virus and Other Domestic Nationally Notifiable Arboviral Diseases — United States, 2020](#) (06 May 2022)

"What is already known about this topic? West Nile virus is the leading cause of domestically acquired arboviral disease. Other arboviruses cause sporadic cases and outbreaks, resulting in substantial morbidity and mortality.

What is added by this report? In 2020, the national incidence of neuroinvasive West Nile virus disease was 59% lower than the median annual incidence during 2010–2019. However, the neuroinvasive disease incidence for other domestic arboviral diseases was higher in 2020 than the median annual incidence for the preceding 10 years.

What are the implications for public health practice? Health care providers should consider arboviral infections in patients with aseptic meningitis or encephalitis during periods when mosquitoes and ticks are active, perform recommended diagnostic testing, and promptly report cases to public health authorities to guide prevention strategies and messaging."

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